REMARKS/ARGUMENTS

Claims 1-10 and 26-36 are active in this application.

The publications cited in the Office Action do not describe or suggest the invention claimed. Specifically, Parce (U.S. patent no. 6,613,513) employs a fundamentally different principal for determining a sequence of a nucleic acid molecule compared to the invention claimed in the present application.

In Parce, the method involves a chain terminating nucleotide moiety, see the Abstract ("*nucleotide analogs comprising 3' blocking groups are used*"), col. 9, lines 39-41 ("*primer strands are terminated by the addition of a nucleotide comprising a blocking group*"), col. 11, lines 50-56 ("*The chain terminating nucleotides typically contain a blocking group on the 3'OH. A "blocking group" typically* ***prevents addition of a nucleotide to the 3'terminus*** ..." These types of chain terminating nucleotides are known (see the attached paper by Sanger et al (1977) Proc. Natl. Acad. Sci. USA 74:5463-5467) and are different from those used in the claims.

The claimed methods employ a dye-labeled dNTP or NTP labeled in such a way so as to permit further elongation by incorporating additional dNTPs or NTPs (labeled or un-labeled) at the 3' position of the dye-labeled dNTP or NTP.

In Parce, the nucleotides are blocked at the 3' position (see citations above) and may be fluorescently labeled (col. 15, lines 28-35). Contrary to the conclusion stated on page 3 of the Office Action (i.e., "the dye-labeled dNTP or NTP taught by Parce *et al.*, has this ability"), the Parce nucleotides used are clearly chain terminating nucleotides. Before repeating the chain elongation, the blocking group must be removed (see, e.g., col. 14, lines 22-30). In contrast, in the claimed method, the dye-labeled dNTP or NTP is not blocked at

the 3' position (permitting the addition of further nucleotides) and therefore no removal of a blocking moiety is needed.

Innis is relied upon to allege that it would have been obvious to use mineral oil to overlay a solution. However, Innis does not describe the types of dye-labeled nucleotides used in the claimed method nor would one have modified the Parce method to use the types of dye-labeled nucleotides in the claims based on Innis.

On this basis, Applicants request withdrawal of the rejection of Claims 1-4, 7-10, 26-29 and 32-35 under 35 USC 103(a).

Further, while Innis teach overlaying mineral oil to prevent evaporation, this is not the same as entrapping a solution within a hydrophobic liquid. The introduction of the reaction solution containing polymerase, nucleotides etc, in the hydrophobic liquid facilitates the reaction in terms of limiting the reaction to only sites where the nucleotide is immobilized and inhibiting unreacted nucleotides from being adsorbed in inappropriate places, which is disadvantageous in terms of having to wash away unreacted nucleotides. Furthermore, by entrapping the reaction solution (not simply overlaying as in Innis) background signals can be greatly decreased.

In view of these additional points of distinction, Applicants again ask that the 103(a) rejection be withdrawn.

Furthermore, Claims 5 and 30; and Claims 6 and 31 would not have been obvious in view of Parce and Innis combined with Mathies or Anazawa.

Mathies is relied upon to provide the use of confocal fluorescence microscopy to detect fluorescent signals. Matheis does not suggest replacing the chain terminating nucleotide in Parce nor entrapping the reaction solution. Therefore, the combination of these

publications provides no description nor reasonable suggestion to employ the dye-labeled dNTP or NTP coupled with entrapment with hydrophobic liquid as claimed. Withdrawal of the rejection of Claims 5 and 30 under 35 U.S.C. § 103(a) is requested.

Anazawa describe a primer extension reaction using DNA polymerase and four types of NTPs, each of which are differentially labeled (see column 6, lines 27-33 of Anazawa). Anazawa is relied upon to provide the use of lasers to disrupt the dye molecule. Anazawa does not suggest replacing the chain terminating nucleotide in Parce nor entrapping the reaction solution. Therefore, the combination of these publications provides no description nor reasonable suggestion to employ the dye-labeled dNTP or NTP coupled with entrapment with hydrophobic liquid as claimed. Withdrawal of the rejection of Claims 6 and 31 under 35 U.S.C. § 103(a) is requested.

For the foregoing reasons, it is respectfully submitted that this application is now in a condition for allowance. A notice of allowance for Claims 1-10 and 26-36 is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, he is encouraged to contact Applicants' undersigned representative at the below listed telephone number.

Respectfully submitted,

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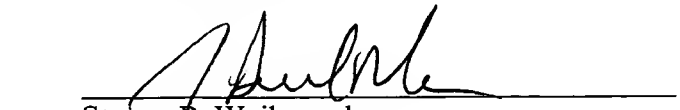

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